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DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ							
<u>L26</u>	I10 and L25	93	<u>L26</u>				
<u>L25</u>	(I2 or I14) and L24	130	<u>L25</u>				
<u>L24</u>	I1 and L22	873	<u>L24</u>				
<u>L23</u>	I15 and L22	2	<u>L23</u>				
<u>L22</u>	(I3 or I5) same I21	2301	<u>L22</u>				
<u>L21</u>	calcium or magnesium or zinc or ca or zn	2311566	<u>L21</u>				
<u>L20</u>	L19 and (I2 or I14)	27	<u>L20</u>				
<u>L19</u>	I17 and I1	90	<u>L19</u>				
<u>L18</u>	115 and L17	0	<u>L18</u>				
<u>L17</u>	15 same 16	121	<u>L17</u>				
<u>L16</u>	12 same 13	95	<u>L16</u>				
<u>L15</u>	particle near (hollow and porous)	145	<u>L15</u>				
<u>L14</u> .	metered dose inhaler or mdi or dry powder inhaler or dpi or atomizer or nebulizer or liquid dose instillation or ldi	45870	<u>L14</u>				
<u>L13</u>	dextrose or galactose or mannitol or mannose or sorbitol or sorbose or lactose or maltose or sucrose or trehalose or raffinose or hydroxyethylstarch or clycodextrin or maltodextrin or sodium chloride or sodium citrate or sodium ascorbate or magnesium gluconate or sodium gluconate or tromethamine hydrochloride or ammonium carbonate or ammonium acetate or ammonium chloride or camphor	297683	<u>L13</u>				
<u>L12</u>	polylactide or cyclodextrin or polyacrylate or methylcollulose or carboxymethylcellulose or polyanhydride or polylactam or dextran or starch or chitin or chitosan or hyaluronic acid or albumin or collagen or gelatin	347713	<u>L12</u>				
<u>L11</u>	sorbitan trioleate or span 85 or sorbitan sesquioleate or sorbitan monooleate or sorbitan monolaurate or polyoxyethylene sorbitan monolaurate or glycerol ester or sucrose ester or poloxamer 188 or pluronic f 68 or poloxamer 407 or pluronic f 127 or poloxamer 338	25054	<u>L11</u>				
<u>L10</u>	pulmonary or lung	73239	<u>L10</u>				
<u>L9</u>	amino acid or monosaccharide or disaccharide or polysaccharide or sodium citrate or citric acid or ammonium carbonate or ammonium acetate or ammonium chloride	321152	<u>L9</u>				
<u>L8</u>	polysaccharide or polyvinyl alcohol or polyvinyl pyrrolidone or polylactide or polyglycolide or polyethylene glycol	240217	<u>L8</u>				
<u>L7</u>	nicotine or human growth hormone or parathyroid hormone or leuprolide or budesonide or tobramycin or albuterol	16528	<u>L7</u>				
<u>L6</u>	calcium or magnesium or zinc or ca or mg or zn	2421673	<u>L6</u>				
<u>L5</u>	dipalmitoylphosphatidylcholine or distearoylphosphatidylcholine	835	<u>L5</u>				
<u>L4</u>	polyvalent cation or divalent cation	7689	<u>L4</u>				
<u>L3</u>	phospholipid	23462	<u>L3</u>				
<u>L2</u>	inhale or inhalation	33074	<u>L2</u>				
<u>L1</u>	particle or particulate	1092046	<u>L1</u>				

**END OF SEARCH HISTORY** 

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                LIPINSKI/CALC added for property searching in REGISTRY
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                 BEILSTEIN: Reload and Implementation of a New Subject Area
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NEWS 15 Apr 09 ZDB will be removed from STN
NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
              CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
              AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
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L2
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             71 S E3 OR E4 OR E2 OR E1
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L7
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PROCESSING COMPLETED FOR L7
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L8
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L9
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=> d ibib abs
L14 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER:
                         1994:680202 CAPLUS
                           Correction of: 1994:297965
DOCUMENT NUMBER:
                         121:280202
                           Correction of: 120:297965
TITLE:
                         About the mechanism of stabilization of fluorocarbon
                         emulsions by mixed fluorocarbon/hydrocarbon additives
AUTHOR (S):
                         Cornelus, Chantal; Krafft, Marie Pierre; Riess,
                         Jean G.
CORPORATE SOURCE:
                         Fac. Sci., Univ. Nice-Sophia Antipolis, Nice, 06108,
                         J. Colloid Interface Sci. (1994), 163(2),
SOURCE:
                         391-4
                         CODEN: JCISA5; ISSN: 0021-9797
DOCUMENT TYPE:
                         Journal
                         English
LANGUAGE:
```

AB Colorimetric detn. of the free phospholipids present in concd. fluorocarbon emulsions indicates that the amt. of phospholipids absorbed at the fluorocarbon/water interface increases when a mixed fluorinated/hydrogenated compd., C6F13C10H21, is added as a stabilizer. The polar head surface area of the phospholipids in emulsions of C8F17Br was reduced from ca. 85.8 .+-. 1.3 .ANG.2 to 74.1 .+-. 1.1 .ANG.2, indicating tighter mol. packing of the surfactant. This effect was not obsd. when C10F21Br was used as a stabilizer, implying that the fluorocarbon/hydrocarbon compd. is located preferentially at the fluorocarbon/hydrocarbon/water interface rather than dispersed throughout the fluorocarbon/hydrocarbon "dowel" mol. is more effective when the dispersed fluorocarbon is linear rather than cyclic.

### => d 2 ibib abs

L14 ANSWER 2 OF 13 USPATFULL

ACCESSION NUMBER: 1999:69741 USPATFULL

TITLE: Methods for the use of stabilized fluorocarbon

emulsions

INVENTOR(S): Weers, Jeffry Greg, San Diego, CA, United

States

Klein, David Henry, Carlsbad, CA, United States Johnson, Cindy Shizuko, Oceanside, CA, United States

PATENT ASSIGNEE(S): Alliance Pharmaceutical Corp., San Diego, CA, United

States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5914352 19990622 <--

APPLICATION INFO.: US 1997-854547 19970512 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1992-967700, filed on 27

Oct 1992, now patented, Pat. No. US 5628930

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Lovering, Richard D. ASSISTANT EXAMINER: Metemaier, Daniel S.

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP

NUMBER OF CLAIMS: 18 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 7 Drawing Page(s)

LINE COUNT: 867

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Storage stable fluorocarbon emulsions having a continuous aqueous phase and a discontinuous fluorocarbon phase, in which the fluorocarbon phase comprises a major amount of a first fluorocarbon or fluorocarbon mixture, and a minor amount of a second fluorocarbon or fluorocarbon mixture, in which the second fluorocarbon has a molecular weight

greater

than that of the first fluorocarbon and the second fluorocarbon includes

a lipophilic moiety in its structure, whereby the second fluorocarbon serves to promote particle size stability in the emulsion while simultaneously providing favorably short organ retention times when administered to animals in vivo.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

- L14 ANSWER 2 OF 13 USPATFULL
- IN Weers, Jeffry Greg, San Diego, CA, United States
- PI US 5914352 19990622
- SUMM . . . first fluorocarbon, and from about 1% to about 20% of the second fluorocarbon. A particularly preferred emulsifier is egg yolk **phospholipid**, and preferred amounts of this emulsifier are 1%-10% w/v. Also preferred are the fluorinated surfactants.
- DRWD FIG. 1 represents accelerated stability testing (T=40.degree. C.) for 90% w/v fluorocarbon, 4% w/V egg yolk **phospholipid** emulsions containing mixtures of perfluoroctyl bromide and perfluorodecyl bromide. The stability of emulsions with 0%, 1%, and 10% w/w perfluorodecyl. . .
- DRWD . . . perfluorodecyl bromide prepared under similar conditions to those of FIG. 1. The emulsions are stabilized by 4% w/v egg yolk phospholipid. (Note the emulsion particle diameters as reported on the Figures are not corrected for the vesicle fraction which shows up. . .
- DRWD FIG. 3 represents accelerated stability testing (T=40.degree. C.) for 60% w/v fluorocarbon, 4% w/v egg yolk **phospholipid** emulsions containing mixtures of perfluoroctyl bromide and perfluorodecyl bromide. The stability of emulsions with 0% and 10% w/w perfluorodecyl bromide. . .
- DRWD FIG. 4(a,b) represents a plot of percent mouse lethality vs. dose (ml/kg) for a 3% egg yolk **phospholipid**, 90% w/v. fluorocarbon emulsion containing 90%/10% w/w perfluoroctyl bromide/perfluorodecyl bromide. The LD.sub.50 of this emulsion is approximately 48 ml/kg.
- DETD . . . added fluorocarbon(s) are excreted at a rate which is physiologically acceptable. Stable fluorocarbon emulsions with particle sizes as small as ca. 0.1 .mu.m may be prepared, with good particle size stability. Surprisingly, emulsions of the present invention may be stored with. . .
- DETD Lecithin is a **phospholipid** that has frequently been used as a fluorocarbon emulsifying agent, as is more fully described in U.S. Pat. No. 4,865,836.. . .
- DETD A reference emulsion containing 90 g PFOB, 4 g egg yolk phospholipid (EYP), and physiological levels of salts and buffers was prepared by high pressure homogenization according to the method of Long. . .
- DETD . . . to 10% w/w of perfluorodecyl bromide added as a stabilizer. In FIG. 1 and Table I, "EYP" is egg yolk **phospholipid**, "perflubron" is perfluorooctyl bromide, "PFDB" is perfluorodecyl bromide, and "S" is the rate of particle growth in units of .mu.m.sup.3.
- DETD . . . w/w Perflubron, as the first fluorocarbon, and 10% perfluorodecyl bromide, as the second fluorocarbon, emulsified with 3% w/v egg yolk phospholipid. The LD.sub.50 was approximately 48
- CLM What is claimed is:
  12. The method of claim 1 wherein said emulsifying agent comprises a phospholipid.
  - 13. The method of claim 12 wherein said **phospholipid** comprises from about 0.1% to about 10% w/v.

L14 ANSWER 3 OF 13 USPATFULL

ACCESSION NUMBER: 1999:58923 USPATFULL

Stable reverse and multiple fluorocarbon emulsions TITLE:

INVENTOR(S):

Riess, Jean G., Nice, France Krafft, Marie-Pierre, Nice, France

Alliance Pharmaceutical Corp., San Diego, CA, United PATENT ASSIGNEE(S):

States (U.S. corporation)

KIND NUMBER DATE

PATENT INFORMATION: US 5904933 19990518 <--

19950607 (8) US 1995-478824 APPLICATION INFO.:

> NUMBER DATE \_\_\_\_\_\_

PRIORITY INFORMATION: FR 1994-7068 19940609

DOCUMENT TYPE: Utility Granted FILE SEGMENT:

ASSISTANT EXAMINER: Page, Thurman K.
LEGAL REPRESENTATION Faulkner

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP

NUMBER OF CLAIMS: 10 EXEMPLARY CLAIM: 1 LINE COUNT: 661

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Stable reverse water-in-fluorocarbon emulsions and

water-in-fluorocarbon-

in-water multiple emulsions comprising the reverse fluorocarbon emulsions. The reverse emulsions comprise a continuous phase which is a highly fluorinated or perfluorinated compound, a discontinuous aqueous phase and a fluorinated surfactant or mixture of surfactants. The multiple emulsions comprise an aqueous continuous phase and a discontinuous phase comprising globules formed of aqueous droplets dispersed into a highly fluorinated or perfluorinated compound. The emulsions can contain pharmacologically active agents, and are particularly suitable for pulmonary drug delivery.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

#### => d 4 ibib abs

L14 ANSWER 4 OF 13 USPATFULL

ACCESSION NUMBER: 1998:161288 USPATFULL

Treatment and diagnosis of respiratory disorders using TITLE:

fluorocarbon liquids

Faithfull, Nicholas Simon, The Woodlands, England INVENTOR(S):

Weers, Jeffry Greg, San Diego, CA, United

Alliance Pharmaceutical Corp., San Diego, CA, United PATENT ASSIGNEE(S):

States (U.S. corporation)

NUMBER KIND DATE \_\_\_\_\_

PATENT INFORMATION:

US 5853003 19981229 US 1997-910981 19970807 (8) APPLICATION INFO.:

Continuation of Ser. No. US 1996-600407, filed on 12 RELATED APPLN. INFO.:

Feb 1996, now patented, Pat. No. US 5655521 which is a continuation of Ser. No. US 1994-299884, filed on 31

Aug 1994, now patented, Pat. No. US 5490498 which is a continuation of Ser. No. US 1991-695547, filed on 3

May

1991, now abandoned

DOCUMENT TYPE: Utility Granted FILE SEGMENT:

Lewis, Aaron J. PRIMARY EXAMINER:

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear, LLP

NUMBER OF CLAIMS: 34 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT:

The present invention includes a method for treating a patient in need AB of facilitated oxygen delivery through the lungs, additional lung surfactant, removal of material from inside the lung, or inflation of collapsed portions of the lung, comprising the step of introducing into the lung of the patient an effective therapeutic amount of a fluorocarbon liquid, the amount not exceeding the functional residual capacity of the lung of the patient upon exhalation taking into account any positive and expiratory pressure applied to the patient's lung. The method may also comprise the additional step of providing an oxygen-containing breathing gas to the patient while the fluorocarbon liquid is in the lung.

# => d 5 ibib abs

L14 ANSWER 5 OF 13 USPATFULL

ACCESSION NUMBER: 1998:108002 USPATFULL

Gas emulsions stabilized with fluorinated ethers TITLE:

having

low Ostwald coefficients

Kabalnov, Alexey, San Diego, CA, United States INVENTOR(S):

Schutt, Ernest George, San Diego, CA, United

States

Weers, Jeffry Greg, San Diego, CA, United

States

Alliance Pharmaceutical Corp., San Diego, CA, United PATENT ASSIGNEE(S):

States (U.S. corporation)

NUMBER KIND DATE -----

US 5804162 19980908 US 1995-479621 19950607 (8) PATENT INFORMATION: <--

APPLICATION INFO.:

DOCUMENT TYPE: Utility FILE SEGMENT: Granted PRIMARY EXAMINER: Kight, John ASSISTANT EXAMINER: Jones, Dameron

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear LLP

NUMBER OF CLAIMS: 89 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 1599

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Long lasting gas emulsions for ultrasound and magnetic resonance

imaging

contrast enhancement utilize low Ostwald coefficient fluoromono- and fluoropolyether compounds. Gas emulsion preparations are disclosed containing air mixed with perfluorodiglyme (CF.sub.3 (OCF.sub.2

CF.sub.2).sub.2 OCF.sub.3), perfluoromonoglyme (CF.sub.3 OCF.sub.2 CF.sub.2 OCF.sub.3), perfluorodiethylether, C.sub.2 F.sub.5 OC.sub.2 F.sub.5, perfluoroethylmethylether, CF.sub.3 OC.sub.2 F.sub.5, and perfluorodimethylether, CF.sub.3 OCF.sub.3.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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FILE 'CAPLUS, USPATFULL, BIOSIS, EMBASE, MEDLINE' ENTERED AT 14:48:35 ON

11 APR 2002 O S WEER JEFFRY/AU L1E WEERS JEFFRY/AU 89 S E3 OR E1 OR E2 OR E4 OR E5 L2E TARARA THOMAS/AU 71 S E3 OR E4 OR E2 OR E1 L3 E DELLAMARY LUIS/AU 44 S E1 OR E2 OR E3 OR E4 T.4 E RIESS JEAN/AU 1.5 306 S E3 OR E4 OR E5 E SCHUTT ERNEST/AU 64 S E3 OR E4 OR E5 OR E6 1.6 464 S L2 OR L3 OR L4 OR L5 OR L6 L7 385 DUP REM L7 (79 DUPLICATES REMOVED) L8344 S L8 AND PY<2000 L9 216855 S PHOSPHOLIPID OR DIPALMITOYLPHOSPHATIDYLCHOLINE OR L10 DISTEAROYLP L11 3615065 S DIVALENT OR CALCIUM OR CA OR MAGNESIUM OR ZINC OR ZN 19907 S L10(P)L11 L12 0 S L12 AND L9 L13 13 S L9 AND L10 AND L11 L14

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L16 6 L9 AND L10 AND L15

=> d ibib abs

L16 ANSWER 1 OF 6 USPATFULL

ACCESSION NUMBER: 1998:108002 USPATFULL

TITLE: Gas emulsions stabilized with fluorinated ethers

having

low Ostwald coefficients

INVENTOR(S): Kabalnov, Alexey, San Diego, CA, United States
Schutt, Ernest George, San Diego, CA, United

States

Weers, Jeffry Greg, San Diego, CA, United

States

PATENT ASSIGNEE(S): Alliance Pharmaceutical Corp., San Diego, CA, United

States (U.S. corporation)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Kight, John
ASSISTANT EXAMINER: Jones, Dameron

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear LLP

NUMBER OF CLAIMS: 89 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 1 Drawing Figure(s); 1 Drawing Page(s)

LINE COUNT: 1599

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Long lasting gas emulsions for ultrasound and magnetic resonance imaging

contrast enhancement utilize low Ostwald coefficient fluoromono- and fluoropolyether compounds. Gas emulsion preparations are disclosed containing air mixed with perfluorodiglyme (CF.sub.3 (OCF.sub.2 CF.sub.2).sub.2 OCF.sub.3), perfluoromonoglyme (CF.sub.3 OCF.sub.2 CF.sub.2 OCF.sub.3), perfluorodiethylether, C.sub.2 F.sub.5 OC.sub.2 F.sub.5, perfluoroethylmethylether, CF.sub.3 OC.sub.2 F.sub.5, and perfluorodimethylether, CF.sub.3 OCF.sub.3.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

#### => d kwic

L16 ANSWER 1 OF 6 USPATFULL

IN Schutt, Ernest George, San Diego, CA, United States
IN Weers, Jeffry Greg, San Diego, CA, United States

PI US 5804162 19980908

SUMM . . . by a surfactant layer which preferably comprises a first and a second surfactant, the first surfactant consisting essentially of a **phospholipid** or mixture of phospholipids having at least one acyl chain which comprises at least 10 carbon atoms, and comprising at.

DETD It has been found especially suitable for the solution to contain a mixture of surfactants including a hydrophobic phospholipid as a first surfactant and at least one additional more hydrophilic second surfactant. Preferably, the hydrophobic phospholipid has at least one acyl chain with a total of at least about 10 carbon atoms (e.g. a didecancyl phospholipid). In some embodiments, the phospholipid first surfactant will have acyl chains from about 10 or 14 to about 20 or 24 carbon atoms. For example, dipalmitoylphosphatidylcholine (comprising two acyl chains, each comprising 16 carbon atoms) may be used. The acyl chain may be hydrogenated or fluorinated. Other phospholipid head groups are also contemplated. For example, the phosphatidylserines, phosphatidylglycerols, or phosphatidylethanolamines will have

properties

suited to the present invention. Combinations of such phospholipids can also comprise the "first surfactant," as can naturally derived phospholipid products such as egg or soy lecithin, or lung surfactants. In addition, the phospholipid first surfactant may be supplemented with other highly water insoluble surfactants such as sucrose di-, tri-, and tetra-esters. Cholesterol may. . . has

been

found useful in promoting stability when provided in a range from about 0.01 to 0.5 w/w cholesterol to **phospholipid**. Preferably, the acyl chains of the **phospholipid** are saturated, although unsaturated acyl groups are also within the scope of the present invention. The first surfactant is preferably.

- DETD It has been found to be advantageous to use a phospholipid mixture comprising a relatively hydrophobic long acyl chain phospholipid in combination with a shorter chain phospholipid which is more hydrophilic than the first phospholipid. As a specific example, a first phospholipid having acyl chains with 12 or 14 carbon atoms may be provided with a second phospholipid as a co-surfactant having acyl chains with eight or ten carbon atoms.
- DETD It has been found particularly advantageous to provide phospholipid comprising 12 carbon atom acyl chains as either the first or second surfactants. For example, a phospholipid with 12 carbon atom acyl chains may comprise the first surfactant, and a sugar ester or Pluronic compound can comprise the second surfactant. As another option, a phospholipid with 16 carbon atom acyl chains may comprise the first surfactant, and a phospholipid with 12 carbon atom acyl chains may comprise the second surfactant.
- DETD . . . comprise less than 5% w/v of solution. Examples of suitable salts include sodium phosphate (both monobasic and dibasic), sodium chloride, calcium phosphate, and other physiologically-acceptable salts.
- DETD . . . that the present invention have applications beyond ultrasound imaging. Indeed, the invention is sufficiently broad to encompass the use of **phospholipid**-containing gas emulsions in any system, including nonbiological applications.
- DETD Spray Drying of Phospholipid-containing Solution
- DETD . . . F-68 (Serva, Heidelberg, Germany), 1.0% w/v Ryoto Sucrose Stearate S-1670 (Mitsubishi-Kasei Food Corp., Tokyo, Japan), and 0.5% Lipoid E-100-3 hydrogenated **phospholipid** (Ludwigshafen, Germany).
- DETD . . . many approximately 1 micron bubbles could be observed for an appreciable time demonstrates the added stability gained by including a phospholipid in the formula as an additional non-Newtonian viscoelastic surfactant.
- DETD Perfluorodiglyme Gas Emulsion with **Phospholipid**/Poloxamer Surfactant
- DETD Perfluorodiglyme Gas Emulsion with **Phospholipid** Mixture Surfactant
- DETD 0.22% w/v Dipalmitoylphosphatidylcholine (Syngena Ltd., Cambridge, Mass.)
- DETD At these ratios of dipalmitoylphosphatidylcholine to dioctanoylphosphatidylcholine the surfactants form mixed micelles only. Upon reconstitution with 5 ml water, approximately 51 million gas emulsion droplets. . .
- DETD B. **Phospholipid** Mixture Microbubble Formulation ("24b" in Table)
- DETD C. Phospholipid Mixture Microbubble Formulation ("24f" in Table)
- CLM What is claimed is:
  - . 5, wherein the surfactant comprises at least a first and a second surfactant, the first surfactant consisting essentially of a **phospholipid** or mixture of phospholipids having at least one acyl chain which comprises at least 10 carbon atoms, and wherein the.
  - 16. The composition of claim 15, wherein said surfactant comprises a **phospholipid**, a mixture of phospholipids, a phosphocholine, or a lysophospholipid.
  - 18. The composition of claim 17, wherein said surfactant comprises a **phospholipid**, a mixture of phospholipids, a phosphocholine, or a

## lysophospholipid.

### => d 2 ibib abs

L16 ANSWER 2 OF 6 USPATFULL

ACCESSION NUMBER:

1998:101389 USPATFULL

TITLE:

Stabilized gas emulsion containing phospholipid

for ultrasound contrast enhancement

INVENTOR(S):

Trevino, Leo A., San Diego, CA, United States Schutt, Ernest George, San Diego, CA, United

States

Klein, David H., Carlsbad, CA, United States Tarara, Thomas E., San Diego, CA, United

States

Weers, Jeffry G., San Diego, CA, United

States

Kabalnov, Alexey, San Diego, CA, United States

Alliance Pharmaceutical Corp., San Diego, CA, United PATENT ASSIGNEE(S):

States (U.S. corporation)

DATE NUMBER KIND

PATENT INFORMATION:

US 5798091 19980825

APPLICATION INFO.:

US 1995-395680 19950228 (8)

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. US 1994-284083, filed on 1 Aug 1994, now patented, Pat. No. US 5605673 which is a continuation-in-part of Ser. No. US 1993-99953,

filed on 30 Jul 1993, now patented, Pat. No. US

5414600

DOCUMENT TYPE:

Utility

FILE SEGMENT:

Granted

PRIMARY EXAMINER:

Hollinden, Gary E.

LEGAL REPRESENTATIVE:

Knobbe, Martens Olson & Bear, LLP

NUMBER OF CLAIMS:

3.5 17

EXEMPLARY CLAIM:

4 Drawing Figure(s); 2 Drawing Page(s)

NUMBER OF DRAWINGS:

1930

LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A gas emulsion forming composition comprising a dry, hollow, particulate, approximately microspherical material permeated with a gas

or gas mixture, which upon dissolution in aqueous liquid forms a gas emulsion comprising a plurality of bubbles surrounded by a layer of at least a first and a second surfactant, wherein the first surfactant

consists essentially of a phospholipid or mixture of

phospholipids having at least one acyl chain which comprises at least

10

carbon atoms, and comprising at least about 5% w/w of total surfactant, and wherein the second surfactant may or may not be a phospholipid and is more water soluble than the first surfactant; kits for preparing such microbubbles; and methods for using such microbubbles as contrast agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 3 ibib abs

L16 ANSWER 3 OF 6 USPATFULL

ACCESSION NUMBER:

1998:33561 USPATFULL

TITLE:

Hydrocarbon oil/fluorochemical preparations and

methods

of use

INVENTOR(S):

Trevino, Leo A., San Diego, CA, United States

Riess, Jean G., Falicon, France

Dellamary, Luis A., San Marcos, CA, United

States

Krafft, Marie-Pierre, Nice, France

Tarara, Thomas E., San Diego, CA, United

States

PATENT ASSIGNEE(S):

Alliance Pharmaceutical Corp., San Diego, CA, United

States (U.S. corporation)

NUMBER KIND DATE -----

PATENT INFORMATION: PATENT INFORMATION: APPLICATION INFO.: US 5733526 19980331 US 1995-572859 19951214 (8) <--

DOCUMENT TYPE:

FILE SEGMENT:

Utility Granted

PRIMARY EXAMINER: Hollinden, Gary E. ASSISTANT EXAMINER: Hartley, Michael G.

LEGAL REPRESENTATIVE: Knobbe, Martens Olson & Bear, LLP

NUMBER OF CLAIMS: 41

1

EXEMPLARY CLAIM: NUMBER OF DRAWINGS:

4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT:

1633

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Novel hydrocarbon oil/fluorochemical preparations and methods for their use are provided. The preparations, which preferably comprise a fluorophilic dispersing agent, may be in the form of hydrocarbon oil-in-fluorochemical dispersions or in the form of a multiple emulsion comprising a polar liquid continuous phase and are particularly useful for administering bioactive agents. In particular the preparations of the present invention may be used to control the bioavailability and improve the efficacy of lipophilic bioactive agents having limited

solubility in an aqueous physiological environment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

#### => d 4 ibib abs

L16 ANSWER 4 OF 6 USPATFULL

ACCESSION NUMBER: 1998:25263 USPATFULL

Liquid fluorocarbon emulsion as a vascular nitric TITLE:

oxide

reservoir

Flaim, Stephen F., San Diego, CA, United States INVENTOR(S):

Riess, Jean G., Nice, France

<--

Alliance Pharmaceutical Corp., San Diego, CA, United PATENT ASSIGNEE(S):

States (U.S. corporation)

NUMBER KIND DATE -----

US 5726209 19980310 US 1995-501976 19950607 (8) PATENT INFORMATION:

APPLICATION INFO.:

DOCUMENT TYPE: FILE SEGMENT: Utility Granted

PRIMARY EXAMINER: Jarvis, William R. A.

LEGAL REPRESENTATIVE: Knobb, Martens, Olson & Bear, LLP.

NUMBER OF CLAIMS: 14 EXEMPLARY CLAIM:

1 Drawing Figure(s); 1 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 470

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Biocompatible fluorocarbon emulsions are utilized to inhibit the removal

of endogenously produced nitric oxide from the bloodstream, and to thereby inhibit vascular stenosis, vasoconstriction, and any other physiological condition or disorder arising in whole or in part from a deficiency of endogenous nitric oxide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

### => d 5 ibib abs

L16 ANSWER 5 OF 6 USPATFULL

97:61694 USPATFULL ACCESSION NUMBER:

TITLE: Fluoroalkylated amphiphilic ligands, their metallic

complexes and their uses

Riess, Jean G., Falicon, France INVENTOR(S):

Vierling, Pierre, Falicon, France Garelli, Nathalie, Nice, France

Alliance Pharmaceutical Corp., San Diego, CA, United PATENT ASSIGNEE(S):

States (U.S. corporation)

NUMBER KIND DATE

US 5648362 19970715 US 1995-377917 19950125 PATENT INFORMATION:

US 1995-377917 19950125 (8) APPLICATION INFO.:

Division of Ser. No. US 1992-955473, filed on 2 Oct RELATED APPLN. INFO.:

1992, now patented, Pat. No. US 5399694

DATE NUMBER \_\_\_\_\_

FR 1991-12130 19911002 PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: Granted PRIMARY EXAMINER: Reamer, James H.

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear

NUMBER OF CLAIMS: 14 EXEMPLARY CLAIM: 1,7

NUMBER OF DRAWINGS: 5 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 1147

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Fluoroalkylated amphiphilic ligands are derived from aromatic amines of AΒ the bipyridine (I) or phenanthroline (II) types, and form complexes

with

platinum, palladium and ruthenium. ##STR1## In formulae (I) and (II), R.sup.1 and R.sup.2 are independently a hydrogen atom, or a fluoroalkylated or hydrocarbon chain, provided at least one of R.sup.1 and R.sup.2 is a fluoroalkylated chain, and W represents a methylene, ester, ether, carbonyl or amide group.

Fluoroalkylated ligands (I or II) and their complexes can be included in

preparations comprising emulsions, dispersions, gels, or microemulsions,

particularly in preparations for therapeutic use.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

### => d 6 ibib abs

L16 ANSWER 6 OF 6 USPATFULL

ACCESSION NUMBER: 95:25039 USPATFULL

TITLE: Fluoroalkylated amphiphilic ligands and their metallic

complexes

INVENTOR(S): Riess, Jean G., Falicon, France

Vierling, Pierre, Falicon, France Garelli, Nathalie, Nice, France

PATENT ASSIGNEE(S): Application et Transferts de Technologies Avancees,

Nice, France (non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5399694 19950321 <--

APPLICATION INFO.: US 1992-955473 19921002 (7)

NUMBER DATE

PRIORITY INFORMATION: FR 1991-12130 19911002

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Cintins, Marianne M. ASSISTANT EXAMINER: Spivack, Phyllis G.

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear

NUMBER OF CLAIMS: 12 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 5 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 1179

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Fluoroalkylated amphiphilic ligands of bipyridine (I) that form complexes with platinum and palladium are disclosed. ##STR1## wherein R.sup.1 and R.sup.2 are independently a hydrogen atom, or a fluoroalkylated or hydrocarbon chain, provided at least one of R.sup.1 and R.sup.2 is a fluoroalkylated chain, and W represents a methylene, ester, ether, carbonyl or amide group.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

## => d his

(FILE 'HOME' ENTERED AT 14:48:19 ON 11 APR 2002)

FILE 'CAPLUS, USPATFULL, BIOSIS, EMBASE, MEDLINE' ENTERED AT 14:48:35 ON 11 APR 2002

L1 0 S WEER JEFFRY/AU

E WEERS JEFFRY/AU

L2 89 S E3 OR E1 OR E2 OR E4 OR E5

E TARARA THOMAS/AU

L3 71 S E3 OR E4 OR E2 OR E1

E DELLAMARY LUIS/AU

L4 44 S E1 OR E2 OR E3 OR E4

E RIESS JEAN/AU

L5 306 S E3 OR E4 OR E5

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E SCHUTT ERNEST/AU
             64 S E3 OR E4 OR E5 OR E6
L6
            464 S L2 OR L3 OR L4 OR L5 OR L6
L7
            385 DUP REM L7 (79 DUPLICATES REMOVED)
L8
            344 S L8 AND PY<2000
1.9
        216855 S PHOSPHOLIPID OR DIPALMITOYLPHOSPHATIDYLCHOLINE OR
T.10
DISTEAROYLP
L11 3615065 S DIVALENT OR CALCIUM OR CA OR MAGNESIUM OR ZINC OR ZN
        19907 S L10(P)L11
L12
             0 S L12 AND L9
L13
L14
             13 S L9 AND L10 AND L11
       2968284 S DIVALENT OR CALCIUM OR MAGNESIUM OR ZINC OR ZN
L15 ·
              6 S L9 AND L10 AND L15
T-16
=> s 110(p)115
       15510 L10(P) L15
L17
=> s particle or particulate or microparticle
L18 1066122 PARTICLE OR PARTICULATE OR MICROPARTICLE
=> s 118(p)110
          4788 L18(P) L10
L19
=> s 110(s)115
        13978 L10(S) L15
L20
=> s 119 and 120
           501 L19 AND L20
=> s divalent or calcium or magnesium or zinc
      2748462 DIVALENT OR CALCIUM OR MAGNESIUM OR ZINC
=> s 110(s)122
L23
        13798 L10(S) L22
=> s 119 and 123
L24
          496 L19 AND L23
=> s 124(1)(lung or pulmonary)
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L139(L) (LUNG'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L140(L) (LUNG'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L141(L) (LUNG'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L142(L) (LUNG'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L143 (L) (LUNG'
            49 L24(L)(LUNG OR PULMONARY)
L25
=> dup rem 125
PROCESSING COMPLETED FOR L25
             38 DUP REM L25 (11 DUPLICATES REMOVED)
=> d ibib abs
L26 ANSWER 1 OF 38 USPATFULL
                        2002:66665 USPATFULL
ACCESSION NUMBER:
                        Phospholipid-based powders for drug delivery
TITLE:
```

Weers, Jeffry G., Half Moon Bay, CA, UNITED STATES INVENTOR (S):

Tarara, Thomas E., Burlingame, CA, UNITED STATES Dellamary, Luis A., San Marcos, CA, UNITED STATES

Riess, Jean G., Falicon, FRANCE

Schutt, Ernest G., San Diego, CA, UNITED STATES

KIND DATE -----

PATENT INFORMATION:

US 2002037316 A1 20020328 US 2001-851226 A1 20010508 (9) APPLICATION INFO.:

Continuation-in-part of Ser. No. US 2000-568818, filed RELATED APPLN. INFO.:

on 10 May 2000, PENDING

DATE NUMBER

US 2000-208896P 20000602 (60) US 2000-216621P 20000707 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: INHALE THERAPEUTIC SYSTEMS, INC, 150 INDUSTRIAL ROAD,

SAN CARLOS, CA, 94070

NUMBER OF CLAIMS: 51 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 3 Drawing Page(s)

LINE COUNT: 1912

Phospholipid based powders for drug delivery applications are disclosed. The powders comprise a polyvalent cation in an amount

effective to increase the gel-to-liquid crystal transition temperature

of the particle compared to particles without the polyvalent cation. The powders are hollow and porous and are preferably

administered via inhalation.

### => d 2 ibib abs

L26 ANSWER 2 OF 38 USPATFULL

2002:30480 USPATFULL ACCESSION NUMBER:

Phospholipid-based powders for inhalation TITLE:

Weers, Jeffry G., Half Moon Bay, CA, UNITED STATES INVENTOR(S): Tarara, Thomas E., Burlingame, CA, UNITED STATES

Clark, Andrew, Half Moon Bay, CA, UNITED STATES

NUMBER KIND DATE \_\_\_\_\_

PATENT INFORMATION: US 2002017295 A1 20020214 US 2001-888311 A1 20010622 (9) APPLICATION INFO.:

> NUMBER DATE \_\_\_\_\_

PRIORITY INFORMATION: US 2000-216621P 20000707 (60)

DOCUMENT TYPE: Utility FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: INHALE THERAPEUTIC SYSTEMS, INC, 150 INDUSTRIAL ROAD,

SAN CARLOS, CA, 94070

NUMBER OF CLAIMS: 20 EXEMPLARY CLAIM:

2 Drawing Page(s) NUMBER OF DRAWINGS:

1103 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Methods for inhalation are provided. The formulations for inhalation AΒ are

engineered to be highly dispersible and provide rapid absorption of the active agent so delivered, as well as substantially independent emitted doses and lung deposition as functions of device resistance and inspiratory flow rates, respectively. The present invention also provides reductions in the flow rate dependence in lung deposition and improvements in patient reproducibility.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 3 ibib abs

L26 ANSWER 3 OF 38 USPATFULL

2002:22435 USPATFULL ACCESSION NUMBER: Cyclosporiine particles TITLE:

Parikh, Indu, Durham, NC, UNITED STATES INVENTOR(S):

Snow, Robert A., West Chester, PA, UNITED STATES

KIND DATE \_\_\_\_\_ US 2002013271 A1 US 2000-750218 A1 20020131 PATENT INFORMATION: 20001229 APPLICATION INFO.:

(9) Continuation-in-part of Ser. No. US 1998-218080, filed RELATED APPLN. INFO.:

on 22 Dec 1998, GRANTED, Pat. No. US 6228399 Continuation-in-part of Ser. No. US 1996-701483, filed

on 22 Aug 1996, ABANDONED

Utility DOCUMENT TYPE: APPLICATION FILE SEGMENT:

LEGAL REPRESENTATIVE: NIXON & VANDERHYE P.C., 8th Floor, 1100 North Glebe

Road, Arlington, VA, 22201

NUMBER OF CLAIMS: 48 EXEMPLARY CLAIM: 1 1517 LINE COUNT:

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Pharmaceutical compositions containing solid cyclic oligopeptide cyclosporine microparticles are prepared by applying energy input to solid cyclic oligopeptide cyclosporine in the presence of phospholipid and one or more non-ionic, anionic or cationic second surface modifiers. The microparticles consist essentially of a solid cyclic oligopeptide cyclosporine core coated with a combination

of

phospholipid and at least one second surface modifier. The combination of phospholipid and second surface modifier(s) provide volume-weighted mean particle size values of solid cyclic oligopeptide cyclosporine particles that are about 50% smaller than cyclic oligopeptide cyclosporine particles produced in the

presence

of the phospholipid and without the presence of the second surface modifier(s) using the same energy input.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 4 ibib abs

L26 ANSWER 4 OF 38 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:833059 CAPLUS

DOCUMENT NUMBER: 135:362596 TITLE: Phospholipid-based powders for drug delivery

INVENTOR(S): Weers, Jeffry G.; Tarara, Thomas E.; Dellamary, Luis

A.; Riess, Jean G.; Schutt, Ernest G.

PATENT ASSIGNEE(S): Alliance Pharmaceutical Corporation, USA

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE: En FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

```
APPLICATION NO. DATE
     PATENT NO.
                       KIND DATE
     -----
                                                -----
                       A2 20011115 WO 2001-US14703 20010508
     WO 2001085136
         W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
              CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
              SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,
              ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
              BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                        A1 20020103
                                             US 2001-852408 20010509
     US 2002000225
                                             US 2001-888311 20010622
US 2000-568818 A 20000510
                               20020214
     US 2002017295
                          A1
PRIORITY APPLN. INFO.:
                                             US 2000-208896P P 20000602
US 2000-216621P P 20000707
```

Phospholipid-based powders for drug delivery applications are disclosed. The powders comprise a polyvalent cation in an amt. effective to increase the gel-to-liq. crystal transition temp. of the particle compared to particles without the polyvalent cation. The powders are hollow and porous and are preferably administered via inhalation. Thus, an emulsions formulation contained DSPC 7.33, CaCl2 0.67, Perflubron 200, SWFI 400, and leuprolide acetate 2.00 g.

## => d 5 ibib abs

L26 ANSWER 5 OF 38 CAPLUS COPYRIGHT 2002 ACS ACCESSION NUMBER: 2001:152465 CAPLUS

DOCUMENT NUMBER: 134:183531

TITLE: Formulation for spray-drying large porous particles INVENTOR(S): Lipp, Michael M.; Batycky, Richard P.; Caponetti,

Giovanni

PATENT ASSIGNEE(S): Advanced Inhalation Research, Inc., USA

SOURCE: PCT Int. Appl., 35 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

```
PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001013892 A2 20010301 WO 2000-US23118 20000823

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
```

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,

CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-150662P P 19990825

AB Particles having a tap d. less than about 0.4 g/cm3 are formed by spray drying from a colloidal soln. including a carboxylic acid or salt thereof,

a phospholipid, a divalent salt and a solvent such as an aq.-org. solvent. The colloidal soln. can also include a therapeutic, prophylactic or diagnostic agent. Preferred carboxylic acids include at least two carboxyl groups. Preferred phospholipids include phosphatidylcholines, phosphatidylethanolamines, phosphatidylglycerols, phosphatidylserines, phosphatidylinositols and combinations thereof. The particles are suitable for pulmonary delivery. A mixt. comprising dipalmitoyl phosphatidylcholine 66, sodium citrate 20, calcium chloride 10, and albuterol sulfate 4% was prepd. in 70:30 ethanol:water cosolvent system and spry-dried. The median geometric diam. of the resulting particles was 9.2 .mu.m and th mass mean aerodynamic diam. was 2.5 .mu.m.

## => d 6 ibib abs

L26 ANSWER 6 OF 38 USPATFULL

ACCESSION NUMBER: 2001:237498 USPATFULL

TITLE: MEDICAMENT ADMINISTRATION SYSTEM INVENTOR(S): NAGATA, SHUNJI, ASHIYA-SHI, Japan

KANAOKA, ERI, OSAKA-SHI, Japan

	NUMBER	KIND	DATE	
APPLICATION INFO.: U	S 2001055610 S 1999-424959 O 1998-JP2374	A1 A1	20011227 19991206 19980529	(9)

None PCT 102(e) date

PRIORITY INFORMATION: JP 1997-148346
DOCUMENT TYPE: Utility

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: WENDEROTH LIND & PONACK, 2033 K STREET NW, SUITE 800,

WASHINGTON, DC, 20006

NUMBER OF CLAIMS: 22 EXEMPLARY CLAIM: 1 LINE COUNT: 917

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A pharmaceutical formulation to be administered by a medicament administration device, which can maintain high stability of a biological

active substance, is provided. In preparing the pharmaceutical formulation to be administered via mucous membrane, particularly a pharmaceutical formulation to be inhaled by utilizing a jet nebulizer, an ultrasonic nebulizer, a metered dose inhaler, or a dry powder inhaler, the adoption of the step of contacting the biological active substance with liposomes or microspheres in an aqueous medium enables the substance to be highly stabilized.

### => d 6 kwic

L26 ANSWER 6 OF 38 USPATFULL

. . . Among cytokines, interferons are preferred, and interferon .qamma. to be used for curative and prophylactic treatment for virus infections or pulmonary diseases is more preferred.

. . in the body which absorbs a physiological substance are, for SUMM instance, nasal mucous membrane, airway mucous membrane, bronchial mucous membrane, pulmonary mucous membrane and the like.

[0034] Liposome is a closed vesicle comprising double layer SUMM phospholipid membranes, which can retain various biological active substances in internal aqueous layer or phospholipid double layer. Accordingly, extensive studies on liposome as a drug carrier have long been conducted. Preferred particle size of liposome is about 20 nm-3 .mu.m. Lipid microspheres, also called lipid emulsion, are small lipid particles obtained by, for example,

suspending

as

plant oil such as soybean oil in water in the presence of phospholipid such as lecithin. Average particle size of lipid microspheres is preferably about 100 nm-300 nm. It should be noted that other aqueous medium into which.

[0069] Twenty ml of a solution containing 25 .mu.mole of calcium DETD (+) - (Z) - 7 - [(1R, 2S, 3S,

4S) -benzensulfonamidobicyclo[2.2.1]hept-2-yl]-5-

heptanoate dihydrate was introduced into a medicament chamber of an ultrasonic nebulizer. Addition of a liposome suspension (125 .mu.mole

phospholipid) thereto gave a pharmaceutical formulation for a man or an animal.

DETD [0077] Five ml of a solution containing 25 .mu.mole of calcium (+) - (Z) - 7 - [(1R, 2S, 3S,

4S) -benzensulfonamidobicyclo[2.2.1]hept-2-yl]-5-

heptanoate dihydrate was introduced into a medicament chamber of a jet nebulizer. Addition of a liposome suspension (125 .mu.mole as phospholipid) thereto gave a pharmaceutical formulation for a man or an animal.

CLM What is claimed is:

biological active substance is interferon .gamma., and the kit is used for curative or prophylactic treatment for virus infections or pulmonary diseases.

=> d 7ibib abs

'71B1B' IS NOT A VALID FORMAT

In a multifile environment, a format can only be used if it is valid in at least one of the files. Refer to file specific help messages or the STNGUIDE file for information on formats available in individual files.

REENTER DISPLAY FORMAT FOR ALL FILES (FILEDEFAULT): end

#### => d 7 bib abs

L26 ANSWER 7 OF 38 USPATFULL

2001:217988 USPATFULL AN

Stabilized preparations for use in metered dose inhalers ΤI

Weers, Jeffry G., San Diego, CA, United States IN

Schutt, Ernest G., San Diego, CA, United States Dellamary, Luis A., San Marcos, CA, United States Tarara, Thomas E., San Diego, CA, United States Kabalnov, Alexey, Corvallis, OR, United States

PI US 2001046474 A1 20011129 AI US 2001-862764 A1 20010521 (9)

RLI Division of Ser. No. US 1998-218212, filed on 22 Dec 1998, PENDING Continuation of Ser. No. WO 1998-US20615, filed on 29 Sep 1998, UNKNOWN Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998, ABANDONED Continuation-in-part of Ser. No. US 1998-106932, filed on 29 Jun 1998, ABANDONED

US 1997-60337P 19970929 (60)

DT Utility FS APPLICATION

LREP INHALE THERAPEUTIC SYSTEMS, INC, 150 INDUSTRIAL ROAD, SAN CARLOS, CA, 94070

CLMN Number of Claims: 150 ECL Exemplary Claim: 1 DRWN 4 Drawing Page(s)

LN.CNT 2850

PRAI

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Stabilized dispersions are provided for the delivery of a bioactive agent to the respiratory tract of a patient. The dispersions preferably comprise a plurality of perforated microstructures dispersed in a suspension medium that typically comprises a hydrofluoroalkane propellant. As density variations between the suspended particles and suspension medium are minimized and attractive forces between microstructures are attenuated, the disclosed dispersions are particularly resistant to degradation, such as, by settling or flocculation. In particularly preferred embodiments, the stabilized dispersions may be administered to the lung of a patient using a metered dose inhaler.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 8 ibib abs

L26 ANSWER 8 OF 38 USPATFULL

ACCESSION NUMBER: 2001:190709 USPATFULL

TITLE: Stabilized preparations for use in metered dose

inhalers

INVENTOR(S): Weers, Jeffry G., San Diego, CA, United States

Schutt, Ernest G., San Diego, CA, United States Dellamary, Luis A., San Marcos, CA, United States Tarara, Thomas E., San Diego, CA, United States Kabalnov, Alexey, Corvallis, OR, United States

PATENT ASSIGNEE(S): Inhale Therapeutic Systems, Inc., San Carlos, CA,

United States (U.S. corporation)

RELATED APPLN. INFO.: Continuation of Ser. No. WO 1998-US20615, filed on 29

Sep 1998 Continuation-in-part of Ser. No. US 1998-133848, filed on 14 Aug 1998, now abandoned

Continuation-in-part of Ser. No. US 1998-106932, filed

on 29 Jun 1998, now abandoned

DATE NUMBER

------US 1997-60337P 19970929 (60) PRIORITY INFORMATION:

DOCUMENT TYPE: Utility FILE SEGMENT: GRANTED

Bawa, Raj PRIMARY EXAMINER:

Rafa, Michael J., Cagan, Felissa H. LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 17 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 2644

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Stabilized dispersions are provided for the delivery of a bioactive agent to the respiratory tract of a patient. The dispersions preferably comprise a plurality of perforated microstructures dispersed in a suspension medium that typically comprises a hydrofluoroalkane propellant. As density variations between the suspended particles and suspension medium are minimized and attractive forces between microstructures are attenuated, the disclosed dispersions are particularly resistant to degradation, such as, by settling or flocculation. In particularly preferred embodiments, the stabilized dispersions may be administered to the lung of a patient using a metered dose inhaler.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 9 ibib abs

L26 ANSWER 9 OF 38 USPATFULL

ACCESSION NUMBER: 2001:25638 USPATFULL Cyclosporin assay and kit TITLE:

Davalian, Dariush, San Jose, CA, United States INVENTOR(S): Beresini, Maureen H., Moss Beach, CA, United States Alexander, Svetlana, Sunnyvale, CA, United States

Hu, Mae Wan-Leng, Los Altos Hills, CA, United States

Ullman, Edwin F., Atherton, CA, United States

Dade Behring Marburg GmbH, Marburg, Germany, Federal PATENT ASSIGNEE(S):

Republic of (non-U.S. corporation)

NUMBER KIND DATE \_\_\_\_\_\_

US 6190873 B1 20010220 PATENT INFORMATION: US 1995-402296 19950310 (8) APPLICATION INFO.:

Division of Ser. No. US 1993-44561, filed on 7 Apr RELATED APPLN. INFO.: 1993, now abandoned Continuation of Ser. No. US

1990-616116, filed on 20 Nov 1990, now abandoned DOCUMENT TYPE: Utility

FILE SEGMENT: Granted PRIMARY EXAMINER: Ceperley, Mary E.

NUMBER OF CLAIMS: EXEMPLARY CLAIM: LINE COUNT: 3042

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A method of measuring the amount of cyclosporin in a sample suspected AB of

containing cyclosporin is disclosed. A method of inactivating interfering cross-reactive material in an assay for measuring the amount

of cyclosporin in a sample suspected of containing cyclosporin is also

disclosed. Compositions wherein cyclosporin is conjugated to an immunogenic carrier or a label, optionally through a linking group, at an alanine nitrogen atom of the cyclic backbone of cyclosporin are also disclosed. Compositions wherein atiocyclosporin is conjugated, optionally through a linking group, to an immunogenic carrier or a

label

are also disclosed. Where cyclosporin is conjugated to an immunogenic carrier, the conjugates may be used as immunogens for the preparation

of

antibodies which are capable of recognizing cyclosporin. Where atiocyclosporin is conjugated to an immunogenic carrier, the conjugates may be used as immunogens for the preparation of antibodies which are capable of recognizing interfering cross-reactive material but substantially incapable of recognizing cyclosporin or cyclosporin-label conjugates. Where cyclosporin is conjugated to a label, the conjugates may be used as part of a signal producing system in cyclosporin assays. Both the antibodies and label conjugates are useful in the disclosed assay methods.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 10 ibib abs

L26 ANSWER 10 OF 38 USPATFULL

ACCESSION NUMBER: 2001:4289 USPATFULL

TITLE:

Synthesis of glycophospholipid and

peptide-phospholipid

conjugates and uses thereof

INVENTOR(S):

Chaikof, Elliot L., Donwoody, GA, United States

Sun, Lijun, Marietta, GA, United States

PATENT ASSIGNEE(S):

Emory University, Alanta, GA, United States (U.S.

corporation)

NUMBER KIND DATE -----

PATENT INFORMATION:

US 6171614 B1 20010109

APPLICATION INFO.:

US 2000-514348 20000228 (9)

RELATED APPLN. INFO.:

Division of Ser. No. US 1996-729928, filed on 15 Oct

1996, now patented, Pat. No. US 6071532

DOCUMENT TYPE: FILE SEGMENT:

Patent Granted

PRIMARY EXAMINER:

Kishore, Gollamudi S.

LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

2.0

LINE COUNT:

2033

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides glycophospholipid and AΒ peptide-phospholipid conjugates comprising a phospholipid moiety and a saccharide or peptide moiety joined by an ether linkage comprising a secondary or tertiary amine. The conjugate structure of the invention comprises a flexible spacer arm between the phospholipid and saccharide or peptide moieties which, being variable in length, serves to optimize saccharide or peptide bioactivity. This invention further provides a method for the synthesis of such conjugates comprising the step of reductive amination. The method is efficient, economical and provides a high yield of product. Glycophospholipid and peptide-phospholipid conjugates of the invention can be incorporated and, optionally, chemically polymerized in self-assembling systems such as membranes,

bilayers, films, liposomes and the like, and find utility diagnostically

and therapeutically in medical and immuno-biological applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 11 ibib abs

L26 ANSWER 11 OF 38 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:824085 CAPLUS

DOCUMENT NUMBER: 134:9357

TITLE: Method of treating angina and/or anginal equivalents

using phospholipid liposomes

INVENTOR(S): Goldberg, Dennis I.; Williams, Kevin Jon

PATENT ASSIGNEE(S): Talaria Therapeutics, Inc., USA

SOURCE: PCT Int. Appl., 142 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

```
KIND DATE
                                                    APPLICATION NO. DATE
      PATENT NO.
                          A1 20001123
                                                    WO 2000-US12962 20000512
      WO 2000069412
          W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
               CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
                SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
                AZ, BY, KG, KZ, MD, RU, TJ, TM
           RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
                CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                            A1 20020306
                                                    EP 2000-932314
                                                                         20000512
      EP 1183011
           R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
                IE, SI, LT, LV, FI, RO
                                                  US 1999-134140P P 19990514
PRIORITY APPLN. INFO.:
                                                  WO 2000-US12962 W 20000512
```

AB The present invention provides a method of treating angina, e.g., stable angina, unstable angina and variant angina, and/or an anginal equiv. comprising administering a therapeutically effective amt. of a multiplicity of liposomes, and preferably, large liposomes comprised of phospholipids substantially free of sterol to a subject for a treatment period. The method also includes administering an effective amt. of an antianginal drug other than the liposomes. The invention also provides a

method of treating claudication comprising administering a

therapeutically

effective amt. of liposomes. In yet another variant, the invention provides a method of perioperative and/or pre-operative conditioning of a subject comprising administering liposomes. Several other inventions are also described herein. An antianginal drug is selected from the group consisting a nitrate, a beta blocker, a calcium channel antagonist, a coronary vasodilator, a lipid lowering drug, an afterload reducing agent, an inotropic agent, a pre-load reducing agent, and an opiate.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE

**FORMAT** 

=> d 12 ibib abs

L26 ANSWER 12 OF 38 USPATFULL

ACCESSION NUMBER: 2000:124531 USPATFULL

TITLE: Charged lipids and uses for the same INVENTOR(S): Unger, Evan C., Tucson, AZ, United States

PATENT ASSIGNEE(S): ImaRx Pharmaceutical Corp., Tucson, AZ, United States

(U.S. corporation)

PATENT INFORMATION: US 6120751 20000919 APPLICATION INFO.: US 1997-925353 19970908 (8)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1997-823791, filed on 21 Mar 1997 And a continuation-in-part of Ser. No.

US 1997-851780, filed on 6 May 1997 And a

continuation-in-part of Ser. No. US 1997-877826, filed on 18 Jun 1997 And a continuation-in-part of Ser. No.

US 1997-887215, filed on 2 Jul 1997

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Dees, Jose' G.
ASSISTANT EXAMINER: Hartley, Michael G.

LEGAL REPRESENTATIVE: Woodcock Washburn Kurtz Mackiewicz & Norris LLP

NUMBER OF CLAIMS: 20 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 4 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 6059

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to charged lipids, compositions comprising charged lipids, and the use of these compositions in drug delivery, targeted drug delivery, therapeutic imaging and diagnostic

imaging, as well as their use as contrast agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 13 ibib abs

L26 ANSWER 13 OF 38 USPATFULL

ACCESSION NUMBER: 2000:70463 USPATFULL

TITLE: Synthesis of glycophospholipid and

peptide-phospholipid

conjugates and uses thereof

INVENTOR(S): Chaikof, Elliot L., Donwoody, GA, United States

Sun, Lijun, Marietta, GA, United States

PATENT ASSIGNEE(S): Emory University, Atlanta, GA, United States (U.S.

corporation)

PATENT INFORMATION: US 6071532 20000606 APPLICATION INFO.: US 1996-729928 19961015 (8)

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Kishore, Gollamudi S.

LEGAL REPRESENTATIVE: Keil & Weinkauf

NUMBER OF CLAIMS: 16 EXEMPLARY CLAIM: 1 NUMBER OF DRAWINGS: 3 Drawing Figure(s); 3 Drawing Page(s)

LINE COUNT: 2007

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The present invention provides glycophospholipid and peptide-phospholipid conjugates comprising a phospholipid moiety and a saccharide or peptide moiety joined by an ether linkage comprising a secondary or tertiary amine. The conjugate structure of the invention comprises a flexible spacer arm between the phospholipid and saccharide or peptide moieties which, being variable in length, serves to optimize saccharide or peptide bioactivity. This invention further provides a method for the synthesis of such conjugates comprising the step of reductive amination. The method is efficient, economical and provides a high yield of product. Glycophospholipid and peptide-phospholipid conjugates of the invention can be incorporated and, optionally,

chemically polymerized in self-assembling systems such as membranes, bilayers, films, liposomes and the like, and find utility

diagnostically

and therapeutically in medical and immuno-biological applications.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 14 ibib abs

L26 ANSWER 14 OF 38 USPATFULL

ACCESSION NUMBER: 2000:57376 USPATFULL Liposomal products

INVENTOR(S): Kikuchi, Hiroshi, Tokyo, Japan

Yachi, Kiyoto, Tokyo, Japan Hirota, Sadao, Tokyo, Japan

PATENT ASSIGNEE(S): Daiichi Pharmaceutical Co., Ltd., Tokyo, Japan

(non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 6060080 20000509 APPLICATION INFO.: US 1995-409924 19950323 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-7050, filed on 21 Jan 1993, now abandoned which is a continuation-in-part of

Ser. No. US 1991-729266, filed on 12 Jul 1991, now

abandoned

NUMBER DATE

PRIORITY INFORMATION: JP 1990-187370 19900716

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Kishore, Gollamudi S.

LEGAL REPRESENTATIVE: Sughrue, Mion, Zinn, Macpeak & Seas, PLLC

NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 651

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A liposomal aqueous dispersion and method of making the liposomal aqueous dispersion is useful for encapsulation of drugs. The liposomal aqueous dispersion comprises: an aqueous suspension medium; multilamellar liposomes comprising an anionic phospholipid and cholesterol as essential components; neutral phospholipid in a mole ratio of 0 to 40% based on the total amount of said multilamellar liposomes; and a cation moiety-containing water-soluble drug, wherein

the electrolyte concentration of said aqueous suspension medium is not more than 40 mM.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 15 ibib abs

L26 ANSWER 15 OF 38 USPATFULL

ACCESSION NUMBER:

2000:50553 USPATFULL

TITLE:

Cyclosporin immunoassay

INVENTOR(S):

Davalian, Dariush, San Jose, CA, United States Beresini, Maureen H., Moss Beach, CA, United States Alexander, Svetlana, Sunnyvale, CA, United States Hu, Mae Wan-Leng, Los Altos Hills, CA, United States

Ullman, Edwin F., Atherton, CA, United States

PATENT ASSIGNEE(S):

Dade Behring Marburg GmbH, Marburg, Germany, Federal

Republic of (non-U.S. corporation)

NUMBER DATE KIND

PATENT INFORMATION:

US 6054303 20000425 US 1995-401827 19950310

APPLICATION INFO.: RELATED APPLN. INFO.:

Division of Ser. No. US 1993-44561, filed on 7 Apr

1993, now abandoned which is a continuation of Ser.

No.

US 1990-616116, filed on 20 Nov 1990, now abandoned

DOCUMENT TYPE:

Utility

FILE SEGMENT:

Granted

PRIMARY EXAMINER:

Ceperley, Mary E.

LEGAL REPRESENTATIVE:

Gatta, P.

NUMBER OF CLAIMS:

38

EXEMPLARY CLAIM:

LINE COUNT:

2882

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

A method of measuring the amount of cyclosporin in a sample suspected of

containing cyclosporin is disclosed. A method of inactivating interfering cross-reactive material in an assay for measuring the

of cyclosporin in a sample suspected of containing cyclosporin is also disclosed. Compositions wherein cyclosporin is conjugated to an immunogenic carrier or a label, optionally through a linking group, at an alanine nitrogen atom of the cyclic backbone of cyclosporin are also disclosed. Compositions wherein atiocyclosporin is conjugated, optionally through a linking group, to an immunogenic carrier or a

label

are also disclosed. Where cyclosporin is conjugated to an immunogenic carrier, the conjugates may be used as immunogens for the preparation

of

antibodies which are capable of recognizing cyclosporin. Where atiocyclosporin is conjugated to an immunogenic carrier, the conjugates may be used as immunogens for the preparation of antibodies which are capable of recognizing interfering cross-reactive material but substantially incapable of recognizing cyclosporin or cyclosporin-label conjugates. Where cyclosporin is conjugated to a label, the conjugates may be used as part of a signal producing system in cyclosporin assays. Both the antibodies and label conjugates are useful in the disclosed assay methods.

#### CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 16 ibib abs

L26 ANSWER 16 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 1

ACCESSION NUMBER: 2000:285794 CAPLUS

DOCUMENT NUMBER: 133:55105

TITLE: Three-Dimensional Structure of Rat Surfactant Protein

A Trimers in Association with Phospholipid Monolayers

AUTHOR(S): Palaniyar, Nades; McCormack, Francis X.; Possmayer,

Fred; Harauz, George

CORPORATE SOURCE: Division of Pulmonary/Critical Care Medicine

Department of Internal Medicine, University of Cincinnati, Cincinnati, OH, 45267-0564, USA

SOURCE: Biochemistry (2000), 39(21), 6310-6316

CODEN: BICHAW; ISSN: 0006-2960

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

Surfactant protein A (SP-A) is a C-type lectin found primarily in the lung and plays a role in innate immunity and the maintenance of surfactant integrity. To det. the three-dimensional (3D) structure of SP-A in assocn. with a lipid ligand, we have used single particle electron crystallog. and computational 3D reconstruction in combination with mol. modeling. Recombinant rat SP-A, contg. a deletion of the collagen-like domain, was incubated with dipalmitoylphosphatidylcholi ne:egg phosphatidylcholine (1:1, wt/wt) lipid monolayers in the presence of calcium, neg. stained, and examd. by TEM. Images of SP-A-lipid complexes with different angular orientations were used to reconstruct the 3D structure of the protein. These results showed that SP-A subunits readily formed trimers and interacted with lipid monolayers exclusively via the globular domains. A homol.-based mol. model of SP-A was generated and fitted into the electron d. map of the protein. The plane of the putative lipid-protein interface was relatively flat and perpendicular to the hydrophobic neck region, and the cleft region in the middle of the trimer had no apparent charge clusters. Amino acid

residues

that are known to affect lipid interactions, Glu195 and Arg197, were located at the protein-lipid interface. The mol. model indicated that the

hydrophobic neck region of the SP-A did not interact with lipid monolayers  $% \left( 1\right) =\left( 1\right) +\left( 1\right)$ 

but was instead involved in intratrimeric subunit interactions. The glycosylation site of SP-A was located at the side of each subunit, suggesting that the covalently linked carbohydrate moiety probably occupies the spaces between the adjacent globular domains, a location

that

would not sterically interfere with ligand binding.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR

THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

=> d 17 ibib abs

L26 ANSWER 17 OF 38 USPATFULL

ACCESSION NUMBER: 1999:155701 USPATFULL

TITLE: Cochleate delivery vehicles

Gould-Fogerite, Susan, Annandale, NJ, United States INVENTOR(S):

Mannino, Raphael James, Annandale, NJ, United States

PATENT ASSIGNEE(S):

Albany Medical College, Albany, NY, United States

(U.S.

University of Medicine and Dentistry of New Jersey,

Newark, NJ, United States (U.S. corporation)

NUMBER KIND DATE \_\_\_\_\_\_ US 5994318 19991130

PATENT INFORMATION:

19970221

APPLICATION INFO.:

US 1997-803662

RELATED APPLN. INFO.:

Continuation-in-part of Ser. No. WO 1996-US1704, filed on 22 Feb 1996 which is a continuation-in-part of Ser.

No. US 1995-394170, filed on 22 Feb 1995, now

patented,

Pat. No. US 5840707 which is a continuation-in-part of

Ser. No. US 1993-130986, filed on 4 Oct 1993, now

patented, Pat. No. US 5643574

DOCUMENT TYPE:

Utility Granted

FILE SEGMENT: PRIMARY EXAMINER:

Campell, Bruce R.

ASSISTANT EXAMINER:

Nguyen, Dave Trong

LEGAL REPRESENTATIVE:

Sughrue, Mion, Zinn, Macpeak & Seas, PLLC

NUMBER OF CLAIMS: EXEMPLARY CLAIM:

59 1

NUMBER OF DRAWINGS:

9 Drawing Figure(s); 9 Drawing Page(s)

LINE COUNT:

1541

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The instant disclosure relates to cochleates comprising a) a biologically relevant molecule component b) a negatively charged lipid component, and c) a divalent cation component. The cochleate has an extended shelf life, even in a desiccated state. Advantageously, the

cochleate can be ingested. The biologically relevant molecule can be a topical application and an in vitro treatment, a polypeptide a drug, a

nutrient, or a flavor.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 18 ibib abs

L26 ANSWER 18 OF 38 CAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

ACCESSION NUMBER:

2000:147131 CAPLUS

DOCUMENT NUMBER:

132:284178

TITLE:

Sustained release of insulin from insoluble inhaled

particles

AUTHOR(S):

Vanbever, Rita; Ben-Jebria, Abdellaziz; Mintzes, Jeffrey D.; Langer, Robert; Edwards, David A.

CORPORATE SOURCE:

Department of Chemical Engineering, Massachusetts Institute of Technology, Cambridge, MA, USA

Drug Dev. Res. (1999), 48(4), 178-185 SOURCE:

CODEN: DDREDK; ISSN: 0272-4391

PUBLISHER: Wiley-Liss, Inc.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

Conventional slow-acting insulin prepns. for s.c. injection, e.g., suspensions of the complex with protamine and/or zinc, were reformulated as dry powders for inhalation and the insol. aerosol tested for providing sustained insulin plasma levels. Large porous particles made of lactose,

albumin, and dipalmitoylphosphatidylcholine, and incorporating insulin, protamine, and/or zinc chloride were prepd. using spray-drying. Integrity of insulin after spray-drying and insulin insolubilization in spray-dried particles was verified in vitro. The pharmacokinetic profile of the formulation delivered by inhalation and s.c. injection was assessed in vivo in the rat. The formulation process of insulin as dry powders did not alter insulin integrity and did not impede, in most cases, insulin insolubilization by protamine and/or zinc. Large porous insulin particles presented 7 .mu.m mass mean geometric particle diams., 0.1 g/cm3 bulk powder tap densities and theor. aerodynamic diams. suitable for deep lung deposition (in the range of 2.2-2.5 .mu.m). The dry powders exhibited 40% respirable fractions in the Andersen cascade impactor and 58-75% in the Aero-Breather. Insol. inhaled insulin provided sustained insulin plasma levels for half a day, similar to injected insulin, and had a bioavailability of 80.5% relative to s.c. injection of the same formulation.

REFERENCE COUNT:

THERE ARE 30 CITED REFERENCES AVAILABLE FOR 30

THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE

FORMAT

=> d 19 ibib abs

L26 ANSWER 19 OF 38 USPATFULL

1998:147423 USPATFULL ACCESSION NUMBER:

Stabilizing and delivery means of biological molecules TITLE:

Mannino, Raphael James, Annandale, NJ, United States INVENTOR(S):

Gould-Fogerite, Susan, Annandale, NJ, United States

Albany Medical College, Albany, NY, United States PATENT ASSIGNEE(S):

(U.S.

corporation)

University of Medicine and Dentistry of New Jersey,

Newark, NJ, United States (U.S. corporation)

KIND DATE NUMBER US 5840707 US 1995-394170 19981124

PATENT INFORMATION: 19950222 (8) APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1993-130986, filed

on 4 Oct 1993

DOCUMENT TYPE: Utility Granted FILE SEGMENT:

Stone, Jacqueline M. PRIMARY EXAMINER: Twomey, Patrick ASSISTANT EXAMINER:

Sughrue, Mion, Zinn, Macpeak, and Seas LEGAL REPRESENTATIVE:

27 NUMBER OF CLAIMS: EXEMPLARY CLAIM:

8 Drawing Figure(s); 8 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 841

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

The instant disclosure relates to cochleates comprising a) a biologically relevant molecule component b) a negatively charged lipid component, and c) a divalent cation component. The cochleate has an extended shelf life, even in a desiccated state. Advantageously, the cochleate can be ingested. The biologically relevant molecule can be a polynucleotide.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

### => d 20 ibib abs

L26 ANSWER 20 OF 38 USPATFULL

ACCESSION NUMBER: 1998:68555 USPATFULL

TITLE: Artificial viral envelopes
INVENTOR(S): Schreier, Hans, Hermitage, TN, United States

Chander, Ramesh, Bombay, India

Stecenko, Arlene A., Nashville, TN, United States
PATENT ASSIGNEE(S): University of Florida Research Foundation, Inc., San

Diego, CA, United States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5766625 19980616
APPLICATION INFO.: US 1995-474814 19950607 (

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-134156, filed on 8

Oct

1993 which is a continuation-in-part of Ser. No. US 1992-923016, filed on 30 Jul 1992, now patented, Pat. No. US 5252348 which is a continuation of Ser. No. US 1890 CONSTANT Filed on 18 Oct 1890 now abandoned

1990-600641, filed on 19 Oct 1990, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Kishore, Gollamudi S.

LEGAL REPRESENTATIVE: Saliwanchik, Lloyd & Saliwanchik

NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
LINE COUNT: 1088

AB The production of artificial viral envelopes by a novel

double-detergent

dialysis technique is disclosed. Specifically exemplified is the production of HIV-1 and RSV viral envelopes. The resulting artificial viral envelopes are essentially identical to the natural virus with regard to characteristics which are relevant to immunogenicity and intracellular transfer of encapsulated material.

### => d 21 ibib abs

L26 ANSWER 21 OF 38 USPATFULL

ACCESSION NUMBER: 1998:54513 USPATFULL TITLE: Artificial viral envelopes

INVENTOR(S): Schreier, Hans, Hermitage, TN, United States

Chander, Ramesh, Bombay, India

Stecenko, Arlene A., Nashville, TN, United States

PATENT ASSIGNEE(S): University of Florida, Gainesville, FL, United States

(U.S. corporation)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1992-923016, filed

on 30 Jul 1992, now patented, Pat. No. US 5252348

which

is a continuation of Ser. No. US 1990-600641, filed on

19 Oct 1990, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Kishore, Gollamudi S.

LEGAL REPRESENTATIVE: Saliwanchik, Lloyd & Saliwanchik

NUMBER OF CLAIMS: 23
EXEMPLARY CLAIM: 1
LINE COUNT: 1050

AB The production of artificial viral envelopes by a novel

double-detergent

dialysis technique is disclosed. Specifically exemplified is the production of HIV-1 and RSV viral envelopes. The resulting artificial viral envelopes are essentially identical to the natural virus with regard to characteristics which are relevant to immunogenicity and interacellular transfer of encapsulated material.

### => d 22 ibib abs

PATENT INFORMATION:

L26 ANSWER 22 OF 38 USPATFULL

ACCESSION NUMBER: 97:94070 USPATFULL

TITLE: Dry chemistry cascade immunoassay and affinity assay

INVENTOR(S): Oberhardt, Bruce J., Raleigh, NC, United States

PATENT ASSIGNEE(S): Cardiovascular Diagnostics, Inc., Durham, NC, United

States (U.S. corporation)

APPLICATION INFO.: US 1996-712370 19960911 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1995-387373, filed on 13 Feb 1995, now patented, Pat. No. US 5601991 which is a continuation of Ser. No. US 1993-18415, filed on 17

Feb

1993, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Housel, James C. ASSISTANT EXAMINER: Wolski, Susan C.

LEGAL REPRESENTATIVE: Oblon, Spivak, McClelland, Maier & Neustadt, p.C.

NUMBER OF CLAIMS: 4 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 20 Drawing Figure(s); 10 Drawing Page(s)

LINE COUNT: 1213

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is described for performing an affinity assay comprising contacting a sample to be assayed for the presence of an analyte with a dry reagent containing the analyte (hapten, antigen, antibody,

receptor,

or complementary polynucleotide) bound to a reaction cascade initiator, an antibody or other binding pair partner reactive with said analyte, and magnetic particles, to form an assay mixture in a reaction chamber, incubating the assay mixture, applying an oscillating or moving static magnetic field to the assay mixture, activating the reaction cascade initiator to initiate a reaction cascade, monitoring the response of

the to

magnetic particles to the oscillating or moving static magnetic field

provide a time varying signal, and determining the analyte concentration

of the sample by analysis of the time varying signal, as well as a kit for performing the assay and a diagnostic system for performing the assay.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 23 ibib abs

L26 ANSWER 23 OF 38 USPATFULL

ACCESSION NUMBER: 97:12332 USPATFULL

TITLE: Dry chemistry cascade immunoassay and affinity assay

INVENTOR(S): Oberhardt, Bruce J., Raleigh, NC, United States

PATENT ASSIGNEE(S): Cardiovascular Diagnostics, Inc., Durham, NC, United

States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5601991 19970211 APPLICATION INFO.: US 1995-387373 19950213 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-18415, filed on 17

Feb

1993, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Hutzell, Paula K. ASSISTANT EXAMINER: Wolski, Susan C.

LEGAL REPRESENTATIVE: Oblon, Spivak, McClelland, Maier & Neustadt, P.C.

NUMBER OF CLAIMS: 86 EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 20 Drawing Figure(s); 10 Drawing Page(s)

LINE COUNT: 1838

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is described for performing an affinity assay comprising contacting a sample to be assayed for the presence of an analyte with a dry reagent containing the analyte (hapten, antigen, antibody,

receptor,

or complementary polynucleotide) bound to a reaction cascade initiator, an antibody or other binding pair partner reactive with said analyte, and magnetic particles, to form an assay mixture in a reaction chamber, incubating the assay mixture, applying an oscillating or moving static magnetic field to the assay mixture, activating the reaction cascade initiator to initiate a reaction cascade, monitoring the response of

the

to

magnetic particles to the oscillating or moving static magnetic field

provide a time varying signal, and determining the analyte concentration

of the sample by analysis of the time varying signal, as well as a kit for performing the assay and a diagnostic system for performing the assay.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 24 ibib abs

L26 ANSWER 24 OF 38 USPATFULL

ACCESSION NUMBER: 96:18811 USPATFULL

TITLE: Percutaneous lymphography

Wolf, Gerald, 5 Hawthorne Rd., Winchester, MA, United INVENTOR (S):

States 01890

NUMBER KIND DATE PATENT INFORMATION: US 5496536 19960305 US 1995-428558 19950425

19950425 (8) APPLICATION INFO.:

Continuation of Ser. No. US 1993-128344, filed on 28 RELATED APPLN. INFO.: Sep 1993, now abandoned which is a continuation of

Ser.

No. US 1992-855570, filed on 23 Mar 1992, now

abandoned

which is a division of Ser. No. US 1990-530034, filed on 29 May 1990, now patented, Pat. No. US 5114703

which

is a continuation-in-part of Ser. No. US 1989-358678,

filed on 30 May 1989, now abandoned

DOCUMENT TYPE:

Utility Granted

FILE SEGMENT: PRIMARY EXAMINER:

Hollinden, Gary E.

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear

NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1 LINE COUNT: 946

Injectable contrast agents of great clinical importance for AΒ lymphography, characterized by non-water soluble particle sizes between

about 5 or 10 nm and about 500 or 900 nm, which have selective distribution to lymph nodes upon percutaneous administration and can be imaged with millimeter resolution. Also disclosed are methods for

performing percutaneous lymphography using these contrast agents.

# => d 25 ibib abs

L26 ANSWER 25 OF 38 USPATFULL

ACCESSION NUMBER: 93:84900 USPATFULL

Artificial viral envelopes TITLE:

Schreier, Hans, Gainesville, FL, United States INVENTOR(S):

Chander, Ramesh, Bombay, India

Stecenko, Arlene A., Gainesville, FL, United States

Univ. of Florida Research Foundation, Inc., PATENT ASSIGNEE(S):

Gainesville, FL, United States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5252348 19931012 US 1992-923016 19920730 (7) APPLICATION INFO.:

RELATED APPLN. INFO.: Continuation of Ser. No. US 1990-600641, filed on 19

Oct 1990, now abandoned

DOCUMENT TYPE: Utility Granted FILE SEGMENT:

PRIMARY EXAMINER: Page, Thurman K. ASSISTANT EXAMINER: Kishore, G. S.

LEGAL REPRESENTATIVE: Saliwanchik & Saliwanchik

5 NUMBER OF CLAIMS: EXEMPLARY CLAIM: 1 731 LINE COUNT:

The production of artificial viral envelopes by a novel AB

double-detergent

dialysis technique is disclosed. Specifically exemplified is the production of HIV-1 and RSV viral envelopes. The resulting artificial viral envelopes are essentially identical to the natural virus with regard to characteristics which are relevant to immunogenicity.

=> d 26 ibib abs

L26 ANSWER 26 OF 38 USPATFULL

ACCESSION NUMBER: 93:25782 USPATFULL

TITLE: Inhibitors of protein kinase C activity as protectors

against septic shock and reducers of ARDS

INVENTOR(S): McKenna, Thomas M., Rockville, MD, United States

Williams, Taffy J., Gaithersburg, MD, United States
The United States of America as represented by the

PATENT ASSIGNEE(S): The United States of America as represented by the

Secretary of the Navy, Washington, DC, United States

(U.S. government)

NUMBER KIND DATE

PATENT INFORMATION: US 1168 19930406 APPLICATION INFO.: US 1991-748307 19910821 (7)

DOCUMENT TYPE: Statutory FILE SEGMENT: Granted

PRIMARY EXAMINER: Stoll, Robert L. ASSISTANT EXAMINER: Anthony, Joseph D.

LEGAL REPRESENTATIVE: Garvert, William C., Spevack, A. David

NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 7 Drawing Figure(s); 4 Drawing Page(s)

LINE COUNT: 873

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An agent and treatment for a subject susceptible to septic shock. The subject is treated with a PKC inhibitor, preferably wit a PKC inhibitor selected from the group consisting of lipid analogues. Preferred among the lipid analogues are sphingosine and its analogues. The inhibitors

of

this invention are administered, preferably by infusion in a suitable pharmaceutical carrier, in a range of 0.1 to 50 mg/Kg body weight preferably in the range of 0.5 to 25 mg/Kg body weight and most preferably in the range of 1 to 5 mg/Kg body weight.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 27 ibib abs

L26 ANSWER 27 OF 38 USPATFULL

ACCESSION NUMBER: 92:40429 USPATFULL

TITLE: Percutaneous lymphography using particulate

fluorocarbon emulsions

INVENTOR(S): Wolf, Gerald L., Winchester, MA, United States

Long, David M., El Cajon, CA, United States

PATENT ASSIGNEE(S): Alliance Pharmaceutical Corp., San Diego, CA, United

States (U.S. corporation)

NUMBER KIND DATE
PATENT INFORMATION: US 5114703 19920519

APPLICATION INFO.: US 1990-530034 19900529 (7)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1989-358678, filed

on 30 May 1989, now abandoned

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Hollrah, Glennon H. ASSISTANT EXAMINER: Hollinden, Gary E.

LEGAL REPRESENTATIVE: Knobbe, Martens, Olson & Bear

NUMBER OF CLAIMS: 24 EXEMPLARY CLAIM: 1,20 LINE COUNT: 959

AB Injectable contrast agents of great clinical importance for

lymphography, characterized by non-water soluble particle sizes between

about 5 or 10 nm and about 500 or 900 nm, which have selective

distribution to lymph nodes upon percutaneous administration and can be

, imaged with millimeter resolution. Also disclosed are methods for performing percutaneous lymphography using these contrast agents.

### => d 28 ibib abs

L26 ANSWER 28 OF 38 USPATFULL

ACCESSION NUMBER: 92:27529 USPATFULL

ACCESSION NUMBER: 92:27529 USPAIRUDD

TITLE: Substituted benzoylurea compounds or their salts,

processes for their production and antitumour

compositions containing them
INVENTOR(S): Haga, Takahiro, Kusatsu, Japan
Yamada, Nobutoshi, Kusatsu, Japan

Yamada, Nobutoshi, Kusatsu, Japan Sugi, Hideo, Kusatsu, Japan

Koyanagi, Toru, Kusatsu, Japan Okada, Hiroshi, Kusatsu, Japan

PATENT ASSIGNEE(S): Ishihara Sangyo Kaisha Ltd., Osaka, Japan (non-U.S.

corporation)

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted

PRIMARY EXAMINER: Shah, Mukund J.

ASSISTANT EXAMINER: Grumbling, Matthew V.

LEGAL REPRESENTATIVE: Oblon, Spivak, McClelland, Maier & Neustadt

NUMBER OF CLAIMS: 12 EXEMPLARY CLAIM: 1 LINE COUNT: 760

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

As ubstituted benzoylurea compound of the formula (I): ##STR1## wherein R.sup.1 is a hydrogen atom, a halogen atom or a nitro group, each of R.sup.2 and R.sup.3 is a hydrogen atom, an alkyl group, --COR.sup.6 (wherein R.sup.6 is an alkyl group or an alkoxy group) or --SO.sub.2 R.sup.6 (wherein R.sup.6 is as defined above), or R.sup.2 and R.sup.3 may form together with the adjacent nitrogen atom a heterocyclic ring,

R.sup.4 is a halogen atom, a substituted or unsubstituted alkyl group,

substituted or unsubstituted alkoxy group, a substituted or unsubstituted alkylthio group or a nitro group, and R.sup.5 is a halogen

atom, a nitro group or a substituted or unsubstituted alkyl group, or its salt.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 29 ibib abs

а

L26 ANSWER 29 OF 38 USPATFULL

ACCESSION NUMBER: 92:14930 USPATFULL

TITLE: Whole blood activated partial thromboplastin time test

and associated apparatus

INVENTOR(S): La Duca, Frank M., East Brunswick, NJ, United States

Marcelino, Eduardo I., Edison, NJ, United States

PATENT ASSIGNEE(S): International Technidyne Corporation, Edison, NJ,

United States (U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 5091304 19920225 APPLICATION INFO.: US 1989-396043 19890821 (7)

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Yarbrough, Amelia Burgess

LEGAL REPRESENTATIVE: Plevy, Arthur L.

NUMBER OF CLAIMS: 25 EXEMPLARY CLAIM: 1 LINE COUNT: 509

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB An activated partial thromboplastin time (APTT) test is described which does not require blood which has been anticoagulated with citrate. The test enables the citrate anticoagulant step to be combined with the contact activation step and hence enables one to employ fresh

non-anticoagulated blood specimens to directly perform the APTT Test.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 30 ibib abs

L26 ANSWER 30 OF 38 USPATFULL

ACCESSION NUMBER: 92:14815 USPATFULL

TITLE: Phospholipid-coated microcrystals: injectable

formulations of water-insoluble drugs

INVENTOR(S): Haynes, Duncan H., 4051 Barbarossa Ave., Miami, FL,

United States 33133

PATENT INFORMATION: US 5091188 19920225 APPLICATION INFO.: US 1990-514012 19900426 (7)

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Page, Thurman K. ASSISTANT EXAMINER: Kishore, G. S.

Nixon & Vanderhye LEGAL REPRESENTATIVE:

NUMBER OF CLAIMS: 18 EXEMPLARY CLAIM:

10 Drawing Figure(s); 9 Drawing Page(s) NUMBER OF DRAWINGS:

LINE COUNT: 1878

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Water-insoluble drugs are rendered injectable by formulation as aqueous suspensions of phospholipid-coated microcrystals. The crystalline drug is reduced to 50 nm to 10 .mu.m dimensions by sonication or other processes inducing high shear in the presence of phospholipid or other membrane-forming amphipathic lipid. The membrane-forming lipid stabilizes the microcrystal by both hydrophobic and hydrophilic interactions, coating and enveloping it and thus protecting it from coalescence, and rendering the drug substance in solid form less irritating to tissue. Additional protection against coalescence is obtained by a secondary coating by additional membrane-forming lipid in vesicular form associated with and surrounding but not enveloping the lipid-encapsulated drug particles. Tissue-compatible formulations containing drug in concentrations up to 40% (w/v) are described. The preparations can be injected intra-lesionally and in numerous other sites, including intra-venous, intra-arterial, intra-muscular, intra-dermal, etc. The disclosure describes examples of formulations

and

pharmacokinetic data with antibiotics, anthelmintic drugs, anti-inflammatory drugs, local and general anesthetics, and biologicals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 31 ibib abs

L26 ANSWER 31 OF 38 USPATFULL

92:14814 USPATFULL ACCESSION NUMBER:

Phospholipid-coated microcrystals: injectable TITLE:

formulations of water-insoluble drugs

Haynes, Duncan H., 4051 Barbarossa Ave., Miami, FL, INVENTOR(S):

United States 33133

NUMBER KIND DATE \_\_\_\_\_\_

PATENT INFORMATION: US 5091187 19920225 APPLICATION INFO.: US 1991-703786 19910521 (7)

RELATED APPLN. INFO.: Division of Ser. No. US 1990-514012, filed on 26 Apr

1990

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

Page, Thurman K. PRIMARY EXAMINER: ASSISTANT EXAMINER: Kishore, G. S. LEGAL REPRESENTATIVE: Nixon & Vanderhye

NUMBER OF CLAIMS: 4 EXEMPLARY CLAIM:

NUMBER OF DRAWINGS: 10 Drawing Figure(s); 9 Drawing Page(s)

LINE COUNT: 1850

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Water-insoluble drugs are rendered injectable by formulation as aqueous suspensions of phospholipid-coated microcrystals. The crystalline drug is reduced to 50 nm to 10 um dimensions by sonication or other

processes

inducing high shear in the presence of phospholipid or other

membrane-forming amphipathic lipid. The membrane-forming lipid stabilizes the microcrystal by both hydrophobic and hydrophilic interactions, coating and enveloping it and thus protecting it from coalescence, and rendering the drug substance in solid form less irritating to tissue. Additional protection against coalescence is obtained by a secondary coating by additional membrane-forming lipid in vesicular form associated with and surrounding but not enveloping the lipid-encapsulated drug particles. Tissue-compatible formulations containing drug in concentrations up to 40% (w/v) are described. The preparations can be injected intra-lesionally and in numerous other sites, including intra-venous, intra-arterial, intra-muscular, intra-dermal, etc. The disclosure describes examples of formulations

and

pharmacokinetic data with antibiotics, anthelmintic drugs, antiinflammatory drugs, local and general anesthetics, and biologicals.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 32 ibib abs

L26 ANSWER 32 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

3

ACCESSION NUMBER: 1990:337869 BIOSIS

DOCUMENT NUMBER: BA90:45888

TITLE: PURIFICATION AND CHARACTERIZATION OF ANNEXIN PROTEINS FROM

BOVINE LUNG.

AUTHOR(S): KHANNA N C; HELWIG E D; IKEBUCHI N W; FITZPATRICK S;

BAJAWA

R: WAISMAN D M

CORPORATE SOURCE: CELL REGULATION GROUP, DEP. MED. BIOCHEM., UNIV. CALGARY,

CALGARY, ALBERTA, CANADA T2N 4N1.

SOURCE: BIOCHEMISTRY, (1990) 29 (20), 4852-4862.

CODEN: BICHAW. ISSN: 0006-2960.

FILE SEGMENT: BA; OLD LANGUAGE: English

AB Calcium-dependent association with a detergent-extracted particulate fraction was used as the first step in the purification of a group of phospholipid binding proteins.

Elution of the detergent-insoluble fraction with excess ethylene glycol bis(.beta.-aminoethyl ether)-N,N,N',N'-tetraacetic acid (EGTA) resulted

in

the release of several soluble proteins, termed calcium -activated proteins or CAPs. In the present paper, we describe the simultaneous purification of these CAPs and characterize their interaction with phospholipid, actin, and calmodulin. Partial sequence analysis has identified the majority of the CAPs as members of the annexin family of calcium and phospholipid binding proteins. Two additional CAPs may be novel proteins, one of which appears to be an annexin protein. All CAPs demonstrated Ca2+-dependent binding to phosphatidylserine vesicles but did not bind to phosphatidylcholine vesicles. The majority of CAPs exhibited Ca2+-dependent binding to F-actin; however, only CAP-III affected the rate of conversion of G-actin to F-actin. The interaction of CAP-III and lipocortin-85 with F-actin resulted in a Ca2+-dependent increase in both light scattering and sedimentation of F-actin under comparatively low centrifugal force. In contrast, only lipocortin-85 caused the formation of F-actin bundles. Although all of the CAPs bound to a calmodulin affinity column in a Ca2+-dependent manner, attempts to demonstrate binding of CAPs to native

calmodulin were unsuccessful. These studies therefore document the similar

behavior of the CAPs toward **phospholipid** and calmodulin but clearly show that F-actin binding or bundling is not a general property

these proteins. The reported purification procedure should allow further comparative studies of these proteins.

## => d 33 ibib abs

L26 ANSWER 33 OF 38 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE

4

ACCESSION NUMBER:

1989:90453 BIOSIS

DOCUMENT NUMBER:

BA87:44589

TITLE:

٥f

DIFFERENTIATION OF HL-60 CELLS IS ASSOCIATED WITH AN

INCREASE IN THE 35-KDA PROTEIN LIPOCORTIN I.

AUTHOR (S):

WILLIAM F; MROCZKOWSKI B; COHEN S; KRAFT A S

CORPORATE SOURCE:

DEP. MED., DIV. HEMATOL./ONCOL., UNIV. ALA. BIRM.,

BIRMINGHAM, ALA. 35294, USA.

SOURCE:

J CELL PHYSIOL, (1988) 137 (3), 402-410.

CODEN: JCLLAX. ISSN: 0021-9541.

FILE SEGMENT:

BA; OLD

LANGUAGE:

English

Lipocortin I, a 35-kDa protein, has been detected in terminally differentiated monocytes and neutrophils. This calcium-phospholipid binding proteins appears to be identical to a 35-kDa protein that can serve as a substrate for the EGF-receptor/tryosine kinase. We have used the human myelocytic cell line HL-60 to explore whether differentiation of hematopoietic cells is associated with changes in the level of lipocortin I. We find that differentiation of HL-60 cells toward the macrophage lineage by the addition of phorbol esters or

vitamin

D3 or toward neutrophils with dibutyryl cyclic AMP or dimethyl sulfoxide is accompanied by an increase in the celluar content of lipocortin I. In comparison, treatment of HL-60 cells with bryostatin 1, a compound that activates protein kinase C but does not differentiate HL-60 cells, did

not

effect the level of 35 kDa protein. We have developed a radioimmunoassay to quantitate this protein by using a polyclonal antibody to a synthetic amino terminal peptide of the 35-kDa protein. This antibody recognizes purified pig lung 35-kDa protein as well as a single 35-kDa protein in HL-60 and A-431 cells as determined by Western blotting and immune precipitation. Differentiated HL-60 cells contain 2.6-fold the amount of 35-kDa protein found in undifferentiated HL-60 cells. Our findings that the addition of phorbol esters to HL-60 cells results in an increase in the mRNA for the 35-kDa protein and in an increase in the incorporation of 35S-methionine into the protein suggest that transcriptional activation or increased stability of the mRNA is responsible for the increased rate of synthesis and accumulation of lipocortin I during differentiation of these cells. In the absence of added divalent cations, we have determined that in differentiated HL-60 cells 79% of lipocortin I protein is located in the cytosol while 21% of the total cellular protein is bound to the particulate fraction. The 35-kDa protein can be removed from the particulate fraction by incubation with chelators or treatment with phospholipase A2 or phospholipase C. Addition of the calcium ionophore A23187 to intact differentiate HL-60 cells causes the 35-kDa protein to associate with the particulate fraction of the cell,

suggesting that modulation of intracellular calcium levels may play a role in changing the intracellular location of this protein.

=> d 34 ibib abs

L26 ANSWER 34 OF 38 CAPLUS COPYRIGHT 2002 ACS

1987:211431 CAPLUS

ACCESSION NUMBER: DOCUMENT NUMBER:

106:211431

TITLE:

Calcium.cntdot.calmodulin-dependent protein

kinase II and calcium.cntdot.

phospholipid-dependent protein kinase

activities in rat tissues assayed with a synthetic

**DUPLICATE 5** 

peptide

AUTHOR(S):

Hashimoto, Yoshiaki; Soderling, Thomas R.

CORPORATE SOURCE: Howard Hughes Med. Inst., Nashville, TN, 37232, USA

SOURCE:

Arch. Biochem. Biophys. (1987), 252(2), 418-25 CODEN: ABBIA4; ISSN: 0003-9861

Journal

DOCUMENT TYPE:

English

LANGUAGE: Rat tissue levels of Ca2+-calmodulin-dependent protein kinase II (protein kinase II) and Ca2+-phospholipid-dependent protein kinase

(protein kinase C) were selectively assayed using the synthetic peptide, syntide-2, as substrate. The sequence of syntide-2 (Pro-Leu-Ala-Arg-Thr-

Leu-Ser-Val-Ala-Gly-Leu-Pro-Gly-Lys-Lys) was homologous to

phosphorylation

site 2 in glycogen synthase. The relative Vmax/Km ratios of the known Ca2+-dependent protein kinases for syntide-2 were detd. to be as follows: protein kinase II, 100; protein kinase C, 22; phosphorylase kinase, 2; myosin light-chain kinase, 0.005. The levels of protein kinase II were highest in cerebrum (3.36 units/g tissue) and spleen (0.85 units/g) and lowest in testis (0.05 units/g) and kidney (0.04 units/g). Protein

kinase

II activity was localized predominantly in the 100,000 gparticulate fraction of cerebrum and testis, in the supernatant fraction of heart, liver, adrenal, and kidney, and about equally distributed between particulate and supernatant in spleen and lung. Likewise, protein kinase C activity was highest in cerebrum (0.56 units/g) and spleen (0.47 units/g), and the majority of activity

present in the cytosolic fraction for all tissues measured except for cerebrum and testis in which the kinase activity was equal in both fractions. Finally, the ratios of protein kinase II to protein kinase C were different in various rat tissues and between particulate and supernatant fractions. These results suggest somewhat different functions for these 2 Ca2+-regulated, multifunctional protein kinases.

=> d 35 ibib abs

L26 ANSWER 35 OF 38 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:139500 CAPLUS

DOCUMENT NUMBER: 98:139500

Enzymic properties of phospholipid methylation in TITLE:

rabbit platelets

Mori, Keiichiro; Taniguchi, Shinkichi; Kumada, Kaoru; AUTHOR (S):

Nakazawa, Kinya; Fujiwara, Motokazu; Fujiwara,

Motohatsu

Fac. Med., Kyoto Univ., Kyoto, 606, Japan CORPORATE SOURCE:

SOURCE: Thromb. Res. (1983), 29(2), 215-24 CODEN: THBRAA; ISSN: 0049-3848

DOCUMENT TYPE: Journal LANGUAGE: English

AB The enzymic properties of phospholipid methylation in

particulate fractions of rabbit platelets were examd. by using

S-adenosyl-L-(methyl-3H) methionine as a substrate. The pH optimum for

the

methylation was .apprx.10.5 under Tris-HCl and glycine-NaOH buffer systems. When Tris-HCl buffer was replaced by phosphate buffer, the pH optimum shifted to .apprx.8.0 and the methylation was increased .apprx.3-fold, compared to that for Tris-HCl buffer at pH 8.0. The formation of the 3H-methylated phospholipids was increased by the addn.

of

exogenous phosphatidyl-N-monomethylethanolamine or phosphatidyl-N,N-dimethylethanolamine, intermediates of the biosynthesis of phosphatidylcholine from phosphatidylethanolamine. However, the increase in product formations by the addn. of exogenous intermediates was all but equal under Tris-HCl and phosphate buffer systems at pH 8.0. These results suggest that phosphate ion stimulates the 1st step of the methyltransferase reaction to form phosphatidyl-N-monomethylethanolamine from phosphatidylethanolamine. The methylation in platelets was inhibited

to 30% of the basal value with Ca2+ (0.2 mM). However, Ca2+ showed different effects on the methylation in various tissues.

#### => d 36 ibib abs

L26 ANSWER 36 OF 38 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:466519 CAPLUS

DOCUMENT NUMBER: 99:66519

TITLE: Comparative abilities of lanthanide ions lanthanum

(3+) and terbium (3+) to substitute for calcium in regulating phospholipid

-sensitive calcium-dependent protein kinase

and myosin light chain kinase

AUTHOR(S): Mazzei, Gonzalo J.; Qi, De Fang; Schatzman, Randall

C.; Raynor, Robert L.; Turner, R. Scott; Kuo, J. F.

CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA

SOURCE: Life Sci. (1983), 33(2), 119-29

CODEN: LIFSAK; ISSN: 0024-3205

DOCUMENT TYPE: Journal LANGUAGE: English

AB Although the lanthanide ions La3+ and Tb3+ were only slightly able to

substitute for Ca2+ activation of phospholipid-sensitive

Ca2+-dependent protein kinase (I), they potentiated the stimulatory activity of a suboptimal concn. of Ca2+. In comparison, the lanthanides

were much more effective Ca2+ substitutes for myosin light-chain kinase,

calmodulin-sensitive Ca2+-dependent protein kinase. Both enzymes, however, were inhibited by high concns. of lanthanides, either in the presence or absence of Ca2+. Similar effects of the lanthanides were

also

noted on phosphorylation of endogenous substrates in the particulate fraction of rat brain stimulated by either phosphatidylserine and Ca2+ or calmodulin and Ca2+. The La3+- or Tb3+-stimulated activity as well as the Ca2+-stimulated activity of I was inhibited by various agents, such as trifluoperazine, polymyxin B, cobra cytotoxin I, melittin, and spermine.

#### => d 37 ibib abs

L26 ANSWER 37 OF 38 USPATFULL

ACCESSION NUMBER: 78:21688 USPATFULL

TITLE: Labelled phospholipid spheres for organ visualization

INVENTOR(S): Petkau, Abram, Pinawa, Canada

Pleskach, Stanley Daniel, Beausejour, Canada

PATENT ASSIGNEE(S): The Atomic Energy of Canada Limited, Ottawa, Canada

(non-U.S. corporation)

NUMBER KIND DATE

PATENT INFORMATION: US 4086330 19780425 APPLICATION INFO.: US 1976-685587 19760512 (5)

RELATED APPLN. INFO.: Division of Ser. No. US 1975-539134, filed on 7 Jan

1975, now patented, Pat. No. US 3992513

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Padgett, Benjamin R. ASSISTANT EXAMINER: Nucker, Christine M. LEGAL REPRESENTATIVE: Field, Lawrence I.

NUMBER OF CLAIMS: 8
EXEMPLARY CLAIM: 1
LINE COUNT: 674

AB A carrier is disclosed for diagnostic scanning agents labelled with short-lived radioisotopes for medical organ studies which comprises colloidally dispersed phospholipid material, and also disclosed are new diagnostic scanning agents utilizing the carrier and a radioisotope, preferably .sup.99m Tc, which is in a form which complexes with the carrier. The radioisotope labelling can be carried out directly before use, the carrier in dispersed form being stable for a considerable period of time. Methods of preparation of the scanning agents are also disclosed which provide a material which localizes mainly in the liver after injection, or alternately at least initially in the lungs when an aggregating agent is used during preparation in a specific sequence of steps. Specific organ scans or sequential scanning is thus possible.

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L26 ANSWER 38 OF 38 USPATFULL

ACCESSION NUMBER: 76:62556 USPATFULL

TITLE: Labelled phospholipid material colloidially dispersed

and sized to localize at preselected organs

INVENTOR(S): Petkau, Abram, Pinawa, Canada

Pleskach, Stanley Daniel, Beausejour, Canada
PATENT ASSIGNEE(S): Atomic Energy of Canada Limited, Ottawa, Canada

(non-U.S. corporation)

PATENT INFORMATION: US 3992513 19761116
APPLICATION INFO.: US 1975-539134 19750107 (5)

DOCUMENT TYPE: Utility FILE SEGMENT: Granted

PRIMARY EXAMINER: Padgett, Benjamin R.
ASSISTANT EXAMINER: Nucker, Christine M.
LEGAL REPRESENTATIVE: Field, Lawrence I.

NUMBER OF CLAIMS: 23 EXEMPLARY CLAIM: 1 LINE COUNT: 743

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A carrier is disclosed for diagnostic scanning agents labelled with short-lived radioisotopes for medical organ studies which comprises colloidally dispersed phospholipid material, and also disclosed are new diagnostic scanning agents utilizing the carrier and a radioisotope, preferably .sup.99m Tc, which is in a form which complexes with the carrier. The radioisotope labelling can be carried out directly before use, the carrier in dispersed form being stable for a considerable period of time. Methods of preparation of the scanning agents are also disclosed which provide a material which localizes mainly in the liver after injection, or alternately at least initially in the lungs when an aggregating agent is used during preparation in a specific sequence of steps. Specific organ scans or sequential scanning is thus possible.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> log y COST IN U.S. DOLLARS	SINCE FILE	TOTAL SESSION
FULL ESTIMATED COST	ENTRY 188.65	188.86
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-5.58	-5.58

STN INTERNATIONAL LOGOFF AT 15:08:36 ON 11 APR 2002